REMARKS

Claims 1-45 and 48-51 are pending in the present application. Claims 1, 3, 17 and 19 have been amended. Claims 48-51 are newly added. Claim 1 is an independent claim. Claims 46 and 47 have been withdrawn by the Examiner as being drawn to a nonelected invention.

Applicants thank the Examiner for acknowledging receipt of priority documents under 35 U.S.C. § 119(a)-(d) and for placing them in the file.

I. Specification

The Examiner has noted the use of the trademarks MILLI-Q, MILLEX and NUCLEPORE in the application and has indicated that the trademarks should be capitalized wherever they appear and be accompanied by the generic terminology.

Applicants have amended the specification to capitalize the trademarks, and to insert the "®" and "™" symbols and generic terminology where appropriate. Applicants note that "MycoMeter" appears to have previously been a trademark of Turner Biosystems, but it is not clear if it is presently in use.

II. Claim Objections

The Examiner has objected to claim 3 because of the following informalities: the word "Algae" is misspelled. Applicants have amended claim 3 to correct this error, and respectfully request reconsideration and withdrawal of this objection.

III. Claim Rejections – 35 U.S.C. §112.

A. Claims 1-45.

The Examiner has rejected claims 1-45 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. In particular, the Examiner stated that "[i]t is unclear whether the interaction between the substrate and the contaminants produces one detectable moiety in each instance of interaction or whether the interaction produces multiple detectable moieties derived from both the substrate and the contaminants." [Office Action p. 5].

Applicants have amended claim 1 to recite, in step (b), "contacting the influent side of the filter in the filter device with a liquid vehicle containing at least one substrate, said at least one substrate being one which through interaction with the contaminants produces a detectable moiety." Applicants submit that this clarification overcomes the rejection to claims 1-45 identified by the Examiner, and therefore respectfully request reconsideration and withdrawal of this rejection.

B. Claim 17.

The Examiner has rejected claim 17 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. In particular, the Examiner stated that "[i]t is unclear how a chromogenic (color producing) substrate will produce a fluorescent product since not all chromogens produce substrates which are both colored in visible light as well as fluorescent light." [Office Action p. 6].

Applicants have amended claim 17 to delete the reference to "fluorescent products" and instead recite "wherein the at least one substrate is a fluorogenic or

chromogenic substrate producing blue, green and red products as the detectable moiety." Applicants submit that this overcomes the rejection to claim 17 identified by the Examiner, and therefore respectfully request reconsideration and withdrawal of this rejection.

C. Claim 19.

The Examiner has rejected claim 19 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. In particular, the Examiner stated that "[a] broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired." [Office Action p. 6].

Applicants have amended claim 19 to delete all ranges other than "at the most 100 picomoles," and have added new claims 48-51 to separately claim each of the other ranges. Applicants submit that this overcomes the rejection to claim 19 identified by the Examiner, and therefore respectfully request reconsideration and withdrawal of this rejection.

IV. Claim Rejections – 35 U.S.C. §102.

A. Rejection over Tuompo et al. (U.S. Patent No. 5,714,343).

The Examiner has rejected claims 1-4, 6-7, 10-13, 16-17, 20, 22-28, 35-36 and 40-45 under 35 U.S.C. §102(b) as being anticipated by Tuompo et al. (U.S. Patent No. 5,714,343)(herein "Tuompo '343"). Applicants respectfully traverse this rejection.

Claim 1 recites "allowing the substrate to interact with the contaminants on the influent side of the filter in the filter device for a period of time, which is sufficient to

allow the detectable moiety to be detected in the liquid vehicle." The Examiner states that Tuompo '343 teaches that "the water soluble substrate MTT which is not retained on the fiber can be used for spectrophotometric methods of detection." [Office Action p. 8]. Applicants understand the Examiner's reference to MTT being used in a spectrophotometric method as meeting the above-quoted language of claim 1. Applicants respectfully submit that Tuompo '343 does not teach the use of MTT in a filter-based method, and therefore does not anticipate the claim 1.

First, the method of Tuompo '343 requires the detection of the microorganisms to be done on the filter. For example, Tuompo '343 states that the third step of his method is "monitoring the filter for the formation of a visibly colored product, wherein the formation of a visibly colored product is indicative of the presence of microorganisms in the sample," and explains that "[p]assing the test solution through the filter causes microorganisms on the filter to be 'dyed,' making them immediately detectable." [Tuompo '343 col. 2, lines 6-9; col. 3, lines 4-6 (emphasis added)].

Second, Tuompo '343 distinguishes his invention and the use of MTT, explaining that "[u]sing NBT, bacteria can be identified with rapidity at room temperature by visual inspection and without any separate measuring equipment" while "MTT is water-soluble and thus is not retained on the fiber but it can be used in spectrophotometric methods." [Tuompo '343 col. 3, lines 19-23]. Thus, rather than teaching the use of MTT in his method, Tuompo '343 explains that MTT is not useful in his method because it does not adhere to the filter and cannot be detected through visual inspection without any separate measuring equipment. Although Tuompo '343 states that MTT could be used in a different type of method (*i.e.*, a spectrophotometric method), there is no teaching in Tuompo '343 of any spectrophotometric method that utilizes a filter. Indeed, Tuompo '343 discusses prior art histology slide- or solution-based methods using MTT to "detect living bacteria by observing whether a color

change occurs upon the addition of a material such as . . . methylthiazolyldiphenyl tetrazolium bromide (MTT) . . . which turns red upon reduction." [Tuompo '343 col. 1, lines 24-31].

For at least these reasons, Tuompo '343 does not anticipate claim 1. Because claims 2-4, 6-7, 10-13, 16-17, 20, 22-28, 35-36 and 40-45 each depends, directly or indirectly, from claim 1, Tuompo '343 does not anticipate any of those claims for at least the same reasons that Tuompo '343 does not anticipate claim 1. Applicants therefore respectfully request reconsideration and withdrawal of this rejection.

B. Rejection over Ralls et al. (U.S. Patent No. 5,741,659).

The Examiner has rejected claims 1, 3-4, 6-7, 10-11, 14-17, 20, 22-25, 27-28 and 35-36 under 35 U.S.C. §102(b) as being anticipated by Ralls et al. (U.S. Patent No. 5,741,659)(herein "Ralls '659"). Applicants respectfully traverse this rejection.

Ralls '659 does not teach "allowing the substrate to interact with the contaminants on the influent side of the filter in the filter device for a period of time, which is sufficient to allow the detectable moiety to be detected in the liquid vehicle." Similar to Tuompo '343, Ralls '659 discusses a technique in which bacteria are deposited and detected on a filter, not in a liquid vehicle. For example, Ralls '659 states that "[f]ive µl of an undiluted saliva (or oral rinse) sample are spotted onto a solid phase substrate flow-through filter device," the "spotted filter device surface is washed by adding 1 drop (50 µl) of PBS to the filter surface and letting it drain through," one drop of an enzymatic substrate solution "is then added to the filter surface and allowed to drain through," "2 drops (100 µl) of [a] chemical enhancing reagent are then added to the filter surface and allowed to drain through," and, when "positive for chymotrypsin-like activity, the area where the sample was spotted develops a reddish-purple color which varies in intensity with the amount of

chymotrypsin-like activity present." [Ralls '659 col. 5, line 66-col. 6, line 43 (emphasis added)]. The focus of Ralls '659 is on the filter surface, and nothing in Ralls '659 teaches or suggests "allowing the substrate to interact with the contaminants on the influent side of the filter in the filter device for a period of time, which is sufficient to allow the detectable moiety to be detected in the liquid vehicle."

For at least these reasons, Ralls '659 does not anticipate claim 1. Because claims 3-4, 6-7, 10-11, 14-17, 20, 22-25, 27-28 and 35-36 each depends, directly or indirectly, from claim 1, Ralls '659 does not anticipate any of those claims for at least the same reasons that Ralls '659 does not anticipate claim 1. Applicants therefore respectfully request reconsideration and withdrawal of this rejection.

C. Rejection over Laine et al. (U.S. Patent No. 6,090,573).

The Examiner has rejected claims 1, 3-4, 6-7, 10-11, 14-15, 17, 20, 22-25, 27-28, 31-33 and 35-36 under 35 U.S.C. §102(b) as being anticipated by Laine et al. (U.S. Patent No. 6,090,573)(herein "Laine '573"). Applicants respectfully traverse this rejection.

The Examiner stated that Laine '573 teaches "allowing the substrate to interact with the bacteria on the influent side of the filter for a period of time, detecting the detectable moiety by interrupting (eluting) contact between the substrate and detect reagent bound bacteria by evacuating the product from influent to effluent side of the filter." [Office Action p. 12]. Applicants respectfully submit that Laine '573 does not teach a substrate that "through interaction with the contaminants produces a detectable moiety" or allowing "the detectable moiety to be detected in the liquid vehicle."

First, in Laine '573 a detectable moiety is not produced through interaction of a substrate with the contaminants. Laine '573 binds an enzyme conjugate such as

"lysozyme-alkaline phosphatase conjugate" to the "bacteria, fungi, and/or cell wall degradative products" on the filter. [Laine '573 col. 46, lines 7-13]. Then, the "presence or amount of bacteria or fungi in the biological sample is visualized by adding about 1 ml of an alkaline phosphatase substrate, (i.e., 1.5 mM bromo-chloro-indolyl phosphate in 1.0 M diethanolamine containing 0.5 mM magnesium chloride, pH 9.6), and incubating until color appears." [Laine '573 col. 46, lines 13-18]. Similarly, in the second dot-blot assay, a lysozyme horseradish peroxidase conjugate is bound to the sample components and then a horseradish peroxidase substrate (4-amino-antipyrene) is added and cleaved to form a colored precipitate. [Laine '573 col. 46, lines 22-30]. Thus, in Laine '573 the interaction producing a detectable moiety is between an exogenous enzyme conjugate and an exogenous enzyme substrate, and not between the contaminants and a substrate.

Second, Laine '573 involves introducing the alkaline phosphatase substrate in a diethanolamine/magnesium chloride vehicle, and the use of an 80% ethanol solution to elute the blue alkaline phosphatase product from the filter. In contrast, claim 1 recites a detectable moiety that is detected in "the liquid vehicle." "The liquid vehicle" is the vehicle in which the substrate was introduced (*e.g.*, claim 1 recites "contacting the influent side of the filter in the filter device with a liquid vehicle containing at least one substrate")(emphasis added). Thus, Laine teaches elution and detection with a vehicle separate from the vehicle in which the substrate is introduced.

For at least these reasons, Laine '573 does not anticipate claim 1. Because claims 3-4, 6-7, 10-11, 14-15, 17, 20, 22-25, 27-28, 31-33 and 35-36 each depends, directly or indirectly, from claim 1, Laine '573 does not anticipate any of those claims for at least the same reasons that Laine '573 does not anticipate claim 1. Applicants therefore respectfully request reconsideration and withdrawal of this rejection.

V. Claim Rejections – 35 U.S.C. §103.

A. Rejection Over Tuompo '343.

The Examiner has rejected claims 1-7, 10-13, 16-17, 20, 22-30, 35-36 and 40-45 under 35 U.S.C. §103(a) as being unpatentable over Tuompo et al. (U.S. Patent No. 5,714,343). Applicants respectfully traverse this rejection.

As discussed above, Tuompo '343 fails to teach allowing the detectable moiety to be detected in the liquid vehicle. Instead, Tuompo'343 teaches "monitoring the filter for the formation of a visibly colored product," and explains that MTT and other water-soluble chromogenic agents are not useful in his method. Indeed, Tuompo '343 teaches away from the use of MTT or other water-soluble chromogenic agents because they are not retained on the fiber and cannot be detected through visual inspection without any separate measuring equipment. Further, the use of MTT or other water-soluble chromogenic agent would render Tuompo's invention inoperable for its intended purpose. *See, e.g., Tec Air, Inc. v. Denso Mfg. Mich., Inc.*, 192 F.3d 1353, 52 USPQ 2d 1294 (Fed. Cir. 1999)("If when combined, the references would produce a seemingly inoperative device, then they teach away from the combination").

For at least these reasons, claim 1 is not rendered obvious by Tuompo '343. Because claims 2-7, 10-13, 16-17, 20, 22-30, 35-36 and 40-45 each depends, directly or indirectly, from claim 1, Tuompo '343 does not render any of those claims obvious for at least the same reasons that Tuompo '343 does not render claim 1 obvious. Applicants therefore respectfully request reconsideration and withdrawal of this rejection.

B. Rejection Over Tuompo '343 and Koumura et al. (U.S. Patent No. 4,591,554).

The Examiner has rejected claims 1-7, 10-13, 16-18, 20, 22-30, 35-38 and 40-45 under 35 U.S.C. §103(a) as being unpatentable over Tuompo et al. (U.S. Patent No. 5,714,343) in view of Koumura et al. (U.S. Patent No. 4,591,554)(herein "Koumura '554"). Applicants respectfully traverse this rejection.

As discussed above, Tuompo '343 fails to teach or suggest allowing the detectable moiety to be detected in the liquid vehicle, and, indeed, teaches away from the use of MTT or other water-soluble chromogenic agents because they are not retained on the fiber and cannot be detected through visual inspection without any separate measuring equipment. The Examiner cites Koumura '554 for "a method wherein a liquid sample of viable microorganisms (bacteria, fungi, etc.) are contacted with methylumbelliferyl derivatives in a liquid vehicle that upon hydrolysis by enzymes characteristic to the microorganisms form fluorescent products which are measured directly in the liquid vehicle." [Office Action p. 16]. Applicants respectfully submit that nothing in Koumura '554 cures the deficiencies of Tuompo '343.

For at least these reasons, claim 1 is not rendered obvious by Tuompo '343 in view of Koumura '554. Because claims 2-7, 10-13, 16-18, 20, 22-30, 35-38 and 40-45 each depends, directly or indirectly, from claim 1, Tuompo '343 in view of Koumura '554 does not render any of those claims obvious for at least the same reasons that Tuompo '343 in view of Koumura '554 does not render claim 1 obvious. Applicants therefore respectfully request reconsideration and withdrawal of this rejection.

C. Rejection Over Laine '573.

The Examiner has rejected claims 1, 3-4, 6-11, 14-15, 17, 20-25, 27-28, 31-36 and 39 under 35 U.S.C. §103(a) as being unpatentable over Laine et al. (U.S. Patent No. 6,090,573). Applicants respectfully traverse this rejection.

As discussed above, Laine '573 does not teach a substrate that "through interaction with the contaminants produces a detectable moiety" or allowing "the detectable moiety to be detected in the liquid vehicle." Applicants respectfully submit that nothing in Laine '573 suggests that the substrate interact directly with the contaminants or that the detectable moiety be detected in the liquid vehicle. Indeed, Laine suggests the contrary: That the substrate interacts with an exogenous enzyme conjugate bound to the sample components, and that the detection occurs after elution of substrate in a separate and different vehicle.

For at least those reasons, claim 1 is not rendered obvious by Laine '573. Because claims 3-4, 6-11, 14-15, 17, 20-25, 27-28, 31-36 and 39 each depends, directly or indirectly, from claim 1, Laine '573 does not render any of those claims obvious for at least the same reasons that Laine '573 does not render claim 1 obvious. Applicants therefore respectfully request reconsideration and withdrawal of this rejection.

CONCLUSION

Accordingly, in view of the above amendments and remarks, reconsideration of the objections and rejections and allowance of each of claims 1-45 and 48-51 in connection with the present application is earnestly solicited.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicants hereby petition for a one (1) month extension of time for filing a reply to the outstanding Office Action and submit the required $65.00 extension fee herewith.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 08-0750 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. §1.17; particularly, extension of time fees.

Respectfully submitted,

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